

### **REMARKS**

Claims 1-3, 7-11, 13 and 14 are under examination. Claims 4-6 and 12 are withdrawn as being directed to non-elected species. Claim 1 is currently amended. Claim 15 is cancelled. Support for the amendments is found in the specification, for example, at least in Examples 1 and 2.

### **Rejection Under 35 U.S.C. § 103**

Claims 1-3 and 7-11 are rejected under 35 U.S.C. §103(a) as being unpatentable over Kochendoerfer et al. (US 2004/0115774 A1) in view of Ramnarayan et al. (US 2003/0158672 A1). Specifically, the Office Action states, "Regarding claim 1, Kochendoerfer et al. teaches a method of using three dimensional protein structure information (page 15, paragraph 0137), using a module that identifies amino acid positions suitable for attachment of a polymer (page 14, paragraph 0132-page 15, paragraph 0139); identifying possible polymers (page 14, paragraph 0132-page 15, paragraph 0139); and physically making and screening one protein with a polymer attached at the attachment site (page 16, paragraph 0142-page 0156)." Applicants respectfully disagree with this characterization of Kochendoerfer as it relates to the amended Claim 1.

Kochendoerfer does not teach the method generating a protein with a favorable attachment site by the of amended Claim 1. Kochendoerfer is directed to what to attach once a site is chosen, as illustrated by the claims of the published application. For example, Claim 1 of Kochendoerfer as published is:

1. An isolated synthetic bioactive protein having the formula Protein-Un-B-Polymer-J\*, wherein Protein comprises a polypeptide chain of a ribosomally specified protein, said polypeptide chain comprising one or more non-overlapping peptide segments covalently bonded by one or more chemical ligation sites, U is a residue of a unique functional group covalently bonded to a mutually reactive unique functional group of a side chain n of one or more amino acids of one or more of said non-overlapping peptide segments, where n is a discrete integer selected from 1 to 6, B is a branching core having three or more arms that may be the same or different and may be present or absent, Polymer is a substantially non-antigenic water-soluble polymer, and J\* is a pendant group having a net charge under physiological conditions selected from the group consisting of negative, neutral and positive.

In regards to Ramnarayan, the application does not teach a method of generating a protein with a polymeric moiety attached at a favorable attachment site, as illustrated by the claims of the published application. For example, Claim 1 of Ramnarayan as published is:

1. A computer-based method of selecting drug therapies for subjects based on genetic polymorphisms, comprising: obtaining amino acid sequences of a target protein that is the product of a gene exhibiting genetic polymorphisms, wherein the sequences represent different genetic polymorphisms; generating 3-D protein structural variant models from the sequences; computationally docking drug molecules with the target protein models; energetically refining the docked complexes; determining the binding interactions between the drug or potential new drug candidate molecules and the models; and selecting drug therapies based on the drug or drugs that have the most favorable binding interactions with the structural variant models.

Regarding amended Claim 1, Kochendoerfer does not teach or suggest "using a simulation module comprising the steps of: i) computationally attaching a plurality of conformers of each of said polymeric moieties to a plurality of amino acids in said target protein; and ii) disallowing conformers at each of said amino acids on the basis of a distance cutoff," as required by the amended claim. Ramnarayan does not supply this missing limitation.

Claims 13 and 14 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Kochendoerfer et al. (US 2004/0115774 A1) in view of Ramnarayan et al. (US 2003/0158672 A1) as applied to claim 1-3 and 7-11 above, and further in view of Manjula et al. (Bioconjugate (February 2003) Volume 14, pages 464-472).

As discussed above, neither Kochendoerfer nor Ramnarayan teach or suggest "using a simulation module comprising the steps of: i) computationally attaching a plurality of conformers of each of said polymeric moieties to a plurality of amino acids in said target protein; and ii) disallowing conformers at each of said amino acids on the basis of a distance cutoff," as required by the amended claim. Manjula does not teach or suggest this missing limitation either.

Applicants respectfully request the rejection under 35 U.S.C. §103 be withdrawn in light of the current amendments.

**CONCLUSION**

Applicants respectfully submit that the claims are now in condition for allowance and early notification to that effect is respectfully requested. If the Examiner feels there are further unresolved issues, the Examiner is respectfully requested to phone the undersigned at (626) 737-8089.

Respectfully submitted,

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